

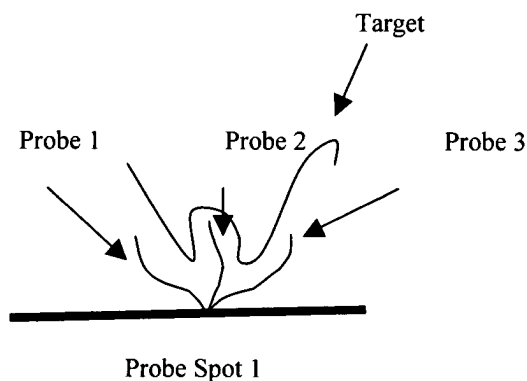
page is captioned **"Version with markings to show changes made."** As such, the above amendments introduce no new matter to the application and their entry by the Examiner is respectfully requested.

The Examiner has objected to the specification for lack of cross reference to the parent provisional application. In view of the above amendment to the specification, this rejection may be withdrawn.

Claims 6, 7, 13, 65, 66 and 72 were rejected under 35 U.S.C. §112, 2<sup>nd</sup> ¶ for use of the term "corresponds to." In view of the above amendments to the claims substituting "binds" for "corresponds" pursuant to the Examiner's rejection, this rejection may be withdrawn.

In the Office Action, Claims 1-11, 13, 16, 53, 59-70, 72, 75 and 77 were rejected under 35 U.S.C. § 102(b) as being anticipated by Adams et al (WO 98/36094).

As amended, each distinct probe oligonucleotide of each spot of the mixture that makes up each probe composition of the claimed arrays must hybridize to the same target nucleic acid strand. As such, if each composition consists of two different oligonucleotide probes, each of the two different oligonucleotide probes must hybridize to the same target strand, and not to different target strands of a duplex structure. Likewise, if the array is made up of probe compositions where each composition consists of three different oligonucleotide probes, each of the three different oligonucleotide probes must hybridize to the same target strand as illustrated below:



Turning now to Adams, this disclosure is directed in part to ways of performing surface bound amplification reactions, e.g., as may be practiced in nucleic acid analyte detection assays. The goal of the methods and devices disclosed in this reference is to produce surface bound amplification products, and then detect these products. In those embodiments where Adams teaches the use of primer pairs to detect a target nucleic acid via surface bound amplification, Adams teaches that the primer pairs hybridize to different strands of a duplex nucleic acid, i.e., to the sense and antisense strand. See page 5, lines 2 to 5, as well as Figure 2 and the description on page 6, lines 7 to 29, where primer pairs are employed that hybridize to different strands of duplex nucleic acid target.

Nowhere is it taught or suggested that the primer pairs hybridize to the same target nucleic acid strand. During the above summarized interview, the Examiner initially asserted that the teachings of Adams at page 6 do indeed disclose a situation where both of the primers hybridize to the same single strand nucleic acid pulled down from solution. However, upon closer reading of the disclosure of page six, it is apparent that what is actually disclosed is a situation where a primer pair is bound to the support surface where the primers of the primer pair do not hybridize to the same single stranded target nucleic acid. In the disclosure of page six, the first primer hybridizes to a nucleic acid from solution. A primer extension product is then produced, called the target nucleic acid, which uses the nucleic acid from solution as template and the first primer as primer. As such, this primer extension product includes the first primer. This primer extension product or target nucleic acid then hybridizes to the second primer in order to form a "bridge." Because the primer extension product is complementary to the initial nucleic acid pulled down from solution, and the second primer hybridizes to the primer extension product, the second primer is identical to a sequence found in the first nucleic acid brought down from sample, and not complementary to it. As such, the first and second primers do not hybridize to the same nucleic acid which is brought down from solution.

The Examiner also expressed concern over the disclosure on page 24 of a detection probe. This part of the disclosure is concerned with the detection of the surface bound amplification products that are the result of Adams' method. Adams discloses that this probe is a detectable label and, upon hybridization to the amplification product, can be used to detect the amplification product. Nowhere is it taught or suggested that this probe is bound to the support surface. Furthermore, it is believed that one would not attach the probe to the surface because if one did so, one would detect a signal on the surface regardless of whether amplification product was present on the surface or not. As such, it is not seen how this teaching of a detection probe teaches or suggests the claimed invention where two or more probes that hybridize to the same single stranded target nucleic acid are bound to the surface of a support.

As such, Adams clearly fails to disclose an array in which each probe spot includes at least two different oligonucleotides that hybridize to the same nucleic acid strand. Accordingly, Adams fails to anticipate the claimed invention and this rejection of Claims 1-11, 13, 16, 53, 59-70, 72, 75 and 77 under 35 U.S.C. § 102(b) as being anticipated by Adams et al (WO 98/36094) may be withdrawn.

Finally, Claims 12, 14, 15, 17, 57, 58, 71, 73, 74 and 76 are rejected under 35 U.S.C. § 103(a) as being obvious over Adams et al (WO 98/36094).

As discussed above, the pending claims now clearly limit the probe compositions to ones in which all of the probes in a given probe composition hybridize to the same target nucleic acid.

In the situations where Adams discusses the use of primer pairs, the primer pairs do not hybridize to the same target nucleic acid strand, but instead hybridize to different strands of a duplex structure. Furthermore, it is not seen how the Adams amplification protocols that employ primer pairs would work if the primers hybridized to the same strand. See Fig. 2 which requires that the two primers hybridize to different strands. The goal of Adams procedure is to produce surface bound amplified amounts of product, i.e., extra copies of an initial target nucleic acid. If the target nucleic acid were to hybridize to two or more primers, surface bound amplified

amounts of the nucleic acid could not be produced. As such, Adams does not suggest the claimed invention.

Accordingly, Adams fails to teach or suggest using two or more primers that hybridize to the same strand, and in fact teaches away from such a structure.

Because Adams fails to teach or suggest the above discussed element of the pending claims, and in fact teaches away from this element, Claims 12, 14, 15, 17, 57, 58, 71, 73, 74 and 76 are not obvious under 35 U.S.C. § 103(a) as over Adams et al (WO 98/36094) and this rejection may be withdrawn.

In view of the attached amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815.

Respectfully submitted,

BOZICEVIC, FIELD & FRANCIS LLP

Date: 4.2.02

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

**In the specification:**

Page 1, immediately beneath the title, please insert:

--CROSS-REFERENCE TO RELATED APPLICATIONS

Pursuant to 35 U.S.C. §119(e), this application claims priority to the filing date of United States Provisional Patent Application Serial No. 60/104,179 filed October 13, 1998, the disclosure of which is herein incorporated by reference.--

**In the claims:**

1. (Amended) An array comprising at least one pattern of probe oligonucleotide spots attached to a surface of a solid support, wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence each attached to said surface of said solid support that hybridize to the same target nucleic acid strand to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides.
6. (Amended) The array according to Claim 5, wherein each probe oligonucleotide spot in said pattern ~~corresponds~~ binds to a different target nucleic acid.
7. (Amended) The array according to Claim 5, wherein two or more probe oligonucleotide spots in said pattern ~~correspond~~ bind to the same target nucleic acid.
13. (Amended) The array according to Claim 1, wherein all of said oligonucleotide spots ~~correspond~~ bind to the same type of target nucleic acid.
57. (Amended) An array comprising a pattern of probe oligonucleotide spots, wherein each probe oligonucleotide spot comprises an oligonucleotide probe composition consisting of a

mixture of 3 to 50 unique oligonucleotides of different sequence and from about 15 to 150 nucleotides in length that are each attached to a surface of a solid support and hybridize to a different region of the same target nucleic acid strand to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides.

58. (Amended) An array comprising a pattern of probe oligonucleotide spots of a density that does not exceed about 400 spots/cm<sup>2</sup>, wherein each probe oligonucleotide spot consists of a mixture of 3 to 20 unique oligonucleotides of different sequence and from about 25 to 100 nucleotides in length that are each attached to a surface of a solid support and hybridize to a different region of the same target nucleic acid strand to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides.

60. (Amended) An array comprising at least one pattern of probe oligonucleotide spots attached to a surface of a solid support, wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that are each attached to said surface of said solid support and cooperatively hybridize to the same target nucleic acid strand to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides.

65. (Amended) The array according to Claim 64, wherein each probe oligonucleotide spot in said pattern ~~corresponds~~ binds to a different target nucleic acid.

66. (Amended) The array according to Claim 64, wherein two or more probe oligonucleotide spots in said pattern ~~correspond~~ bind to the same target nucleic acid.

72. (Amended) The array according to Claim 60, wherein all of said oligonucleotide spots ~~correspond~~ bind to the same type of target nucleic acid.